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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,335	12/12/2003	Doddabele L. Madhavi	BIO 2-016	3791

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EXAMINER	
MAIER, LEIGH C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 04/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/735,335	MADHAVI ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

In view of the appeal brief filed on October 17, 2005, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

4/3/06

SHAOJIA ANNA JIANG, PH.D.
SUPERVISORY PATENT EXAMINER

PROSECUTION REOPENED. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Any rejection or objection not expressly repeated has been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Applicant's submission filed August 29, 2005 the composition claims were amended to include the limitation "having improved bioavailability." However, this limitation is a relative one and must have a benchmark for comparison. Otherwise, the claims are indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Szente et al (J. Incl. Phen., 1998).

Szente discloses the preparation of β–carotene complexed with a variety of cyclodextrins (CDs) and discussed the stabilizing/solubilizing effect of the CD. The reference further discloses a composition comprising β–carotene and β–CD in peanut oil. See Tables V and VI, and sections 5.1-8. Although the reference is not specific about the method of preparing the

complexes, product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. See MPEP 2113.

Claims 1, 2 and 5-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Basu et al (JAOCS, 2001).

Basu discloses a composition comprising high-carotenoid canola oil and cyclodextrins. The composition is not prepared by admixing a freeze-dried CD/carotenoid complex in oil. However, the patentability is determined by the product itself. See discussion above.

Claim Rejections - 35 USC § 103

Claims 1-3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Szente et al (J. Incl. Phen., 1998) in view of Hedges (Chem. Rev., 1998).

Szente teaches as set forth above. As discussed, Szente is silent regarding the specific method of drying the β–carotene/CD complexes. Regarding the use of oil, the reference exemplifies peanut oil, but generally suggests the use of natural plant oils. See Section 6.

Hedges discusses the common methods of drying CD complexes. See section E at page 2036. The reference teaches that several factors, such as drying method must be established for each guest and cyclodextrin.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a complex of β–carotene and cyclodextrin and optimize the method of drying with respect to stabilization and/or solubilization through routine experimentation. Given the correlation between solubility and bioavailability, it would appear more likely than not that one of ordinary skill would arrive at the instant product. Regarding the type of oil, in the absence of unexpected results, it would be within the scope of the artisan to select any appropriate vegetable oil for the preparation of the composition.

In their appeal brief, Applicants cite evidence purporting to demonstrate unexpected results in increased bioavailability of freeze-dried products vs. spray-dried ones by "about several orders of magnitude." However, this is not a comparison of the claimed product, which is the carotenoid/CD complex in oil and not the carotenoid/CD, per se. It is known from Szente, for example, that the properties of a carotenoid/CD complex are modified by the presence of oil. See the paragraph bridging pp 85-6 of Szente. It is further noted that an increase of a single "order of magnitude" would be a ten-fold increase.

Claims 1-3 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000).

Olmedilla teaches the administration of encapsulated carotenoids in oil to humans. See page 449. The reference notes that the bioavailability of carotenoids in supplements is greater than from dietary supplements. See page 454, 2nd col, starting 10 lines from the bottom. The composition does not comprise cyclodextrin.

Pfitzner teaches that complexation of carotenoids (lycopene, lutein and zeaxanthin) with methyl–β–cyclodextrin improves the stability and bioavailability of the carotenoids. See abstract and section 2.2.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a composition comprising a CD/carotenoid complex in oil for human supplementation. One of ordinary skill would be motivated to prepare this composition for the increased bioavailability conferred on the carotenoid by the cyclodextrin. The artisan would reasonably expect success in preparing such a composition. Although Pfitzner does not teach freeze-drying the CD/carotenoid complex, the burden would shift to Applicant to demonstrate that a composition prepared in this manner differs demonstrably from the composition of the invention. It would be within the scope of the artisan to optimize the ratio of cyclodextrin and carotenoid.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000) as applied to claims 1-3 and 6 above, and further in view of Kulevskaya et al (Pharm. Chem. J., 2002).

Olmedilla and Pfitzner teach as set forth above. The references do not teach the addition of lecithin.

Kulevskaya teaches that the absorption of β–carotene significantly increases in the presence of lecithin and other phospholipids. See page 36, 2nd paragraph.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to add lecithin to the composition made obvious by the combination of

Olmedilla and Pfitzner to enhance the bioavailabilty of the carotenoid with a reasonable expectation of success. It would be within the scope of the artisan to optimize the ratio of oil and lecithin through routine experimentation.

Claims 5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000) as applied to claims 1-3 and 6 above, and further in view of Szente et al (J. Incl. Phen., 1998).

Olmedilla and Pfitzner teach as set forth above. The references do not teach the full scope of cyclodextrins recited in the claims.

Szente teaches that the complexation of carotene with a variety of cyclodextrins, including methyl–β–cyclodextrin, stabilizes the carotene. See Tables V and VI and sections 6-8.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to select any of the recited cyclodextrins to modify the composition made obvious by the combination of Olmedilla and Pfitzner, discussed above, for the art disclosed utility of increased stability and bioavailability. One of ordinary skill reasonably expect success in using any of these cyclodextrin because Szente has established functional equivalence between methyl–β–cyclodextrin and the other cyclodextrins.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000) as applied to claims 1-3 and 6 above, and further in view of Sharper (Manufacturing and Formulation, 2001 – retrieved 3/30/06 at http://www.samedanltd.com/members/archives/PMPS/Autumn2001/PeterSharper.htm).

Olmedilla and Pfitzner teach as set forth above. Olmedilla is silent regarding the specific type of capsule used, although one of ordinary skill would expect the use of a gelatin capsule for this type of application.

Sharper teaches that soft gelatin capsules offer several advantages for use with compounds of poor bioavailability, including improved therapeutic effect, lower cost, etc. See entire reference, particularly 2nd page at 1st and 7th full paragraphs.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the composition made obvious by the combination of Olmedilla and Pfitzner, discussed above, by the use of a soft gelatin capsule.

Claims 8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000), and further in view of Szente et al (J. Incl. Phen., 1998), as applied to claims 1-3 and 5-7 above, and further in view of Kulevskaya et al (Pharm. Chem. J., 2002) and Sharper (Manufacturing and Formulation, 2001 – see link above.)

The cited references are discussed above. All of the references are concerned with increasing the bioavailability of carotenoids specifically or poorly absorbed compounds generally (Sharper).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare the carotenoid/CD product recited in the claims. Although the claims have a number of limitations, these are all drawn to additions/modifications to carotenoids that have been disclosed in the art as being beneficial in improving the bioavailability of this

therapeutic agent. One of ordinary skill would be motivated to make these additions/modifications, discussed above, for the combined beneficial effects with a reasonable expectation of success.

Claims 11-13, 15-17 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000), Sharper (Manufacturing and Formulation, 2001 – see link above) and Mele et al (Carbohyd. Res., 2002).

Odmedilla, Pfitzner and Harper teach as set forth above. The references do not teach the preparation of a carotenoid/CD complex by freeze-drying.

Mele teaches the preparation of lycopene/CD complexes that are isolated by freeze-drying. See entire reference, particularly section 3.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a gelatin-encapsulated composition comprising a carotenoid/CD complex in oil for human consumption, as discussed above, for the expected improved bioavailability. It would be within the scope of the artisan to select any known method for drying a prepared carotenoid/CD complex with a reasonable expectation of success. In the absence of unexpected results, one of ordinary skill would be motivated to select freeze-drying because Mele had taught that this method has utility in the preparation of such complexes. The data purporting to demonstrate unexpected results are addressed above.

Claims 14, 18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olmedilla et al (Clin. Sci., 2002) in view of Pfitzner et al (BBA, 2000), Sharper (Manufacturing

and Formulation, 2001 – see link above) and Mele et al (Carbohyd. Res., 2002), as applied to claims 11-13, 15-17 and 19 above, and further in view of Kulevskaya et al (Pharm. Chem. J., 2002).

The references teach as set forth above. The references do not teach the addition of lecithin to the product formed.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the process made obvious by the combination of references set forth above by the addition of lecithin. One of ordinary skill would be motivated to add lecithin for the increased bioavailability taught by Kulevskaya with a reasonable expectation of success.

Double Patenting

Claims 1-3 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3 and 9 of copending Application No. 10/309,999. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reference claims are drawn to a carotenoid/CD complex coated with oil. The reference claims do not require a freeze-dried product or any particular range of molar ratios. However, the description of the reference invention specifically suggests freeze-drying and carotenoid/CD *weight* ratios of 1:3 to 1:20. Given that the weight of β–cyclodextrin is about twice that of β–carotene, there would be significant overlap in these ranges. Applicants have stated in a declaration filed May 2, 2005 that the freeze-drying method had not been reduced to practice. This is not persuasive, as it remains described and claimed in the co-pending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (571) 273-8300.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more. Information regarding the status of an application may be obtained from the Patent Application Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished application is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

Leigh C. Maier

Leigh C. Maier
Primary Examiner
March 31, 2006